AD-A101 820 AIR FORCE INST OF TECH WRIGHT-PATTERSON AFB OH F/G 6/10
BODY FAT AS A FACTOR IN TOLERATING EXPOSURE TO TETRACHLORETHYLE--ETC(U)
JUN 80 K KLINT
UNCLASSIFIED AFIT-CI-80-65T NL

1 OF 1
AD
A101820

END
DATE
FILMED
8-81
DTIC

UNCLASS

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

AD A101820

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 80-65T	2. GOVT ACCESSION NO. AD-A101	3. RECIPIENT'S CATALOG NUMBER 820
4. TITLE (and Subtitle) Body Fat as a Factor in Tolerating Exposure to Tetrachlorethylene Vapor: A Preliminary Study Using Anthropometric Data		5. TYPE OF REPORT & PERIOD COVERED THESIS/~~DISSERTATION~~
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Lt Col Kenneth/Klint		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS AFIT STUDENT AT: University of Texas		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 34
11. CONTROLLING OFFICE NAME AND ADDRESS AFIT/NR WPAFB OH 45433 AFIT-CI-80-65T		12. REPORT DATE June 1980
		13. NUMBER OF PAGES 27
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) Master's thesis		15. SECURITY CLASS. (of this report) UNCLASS
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES APPROVED FOR PUBLIC RELEASE: IAW AFR 190-17 23 JUN 1981		FREDRIC C. LYNCH, Major, USAF Director of Public Affairs Air Force Institute of Technology (ATC) Wright-Patterson AFB, OH 45433
19. KEY WORDS (Continue on reverse side if necessary and identify by block number)		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) ATTACHED		

LEVEL II

DTIC ELECTE JUL 2 1 1981 S D F

81 7 16 009

DTIC FILE COPY

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASS 012200

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

BODY FAT AS A FACTOR IN TOLERATING EXPOSURE TO TETRACHLOROETHYLENE VAPOR: A PRELIMINARY STUDY USING ANTHROPOMETRIC DATA

By

Kenneth Klint, B. A., M. D.

APPROVED:

Alfonso D. Bolzani M.D.

George M. Wallace Jr.

[illegible]

BODY FAT AS A FACTOR IN TOLERATING EXPOSURE TO TETRACHLOROETHYLENE VAPOR: A PRELIMINARY STUDY USING ANTHROPOMETRIC DATA

by

KENNETH KLINT, B. A., M. D.

THESIS

Presented to the Faculty of The University of Texas

Health Science Center at Houston

School of Public Health

in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF PUBLIC HEALTH

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT HOUSTON
SCHOOL OF PUBLIC HEALTH
Houston, Texas
June 1980

ACKNOWLEDGEMENTS

I would like to express my appreciation to the following individuals for their support for this study and thesis:

Dr. Frank Weir, who suggested the research topic;

Dr. Alfonso Holguin, my thesis advisor, who gave valuable advice and encouragement regarding the study design and thesis presentation;

Drs. John Scanlon and George Walker, Jr., my committee members, who contributed comments and suggestions;

Dr. Clayton Eifler, who assisted with the statisical analysis of the data;

Col Thomas Smith, Clinic Commander, Kelly Air Force Base, who made available the facilities of the clinic;

LtCol Donald Higgins, Bioenvironmental Engineer, Kelly Air Force Base, and members of his staff, Wade Pierce and SRA Daniel Bulkley, who assisted in arranging and conducting the survey.

Thesis submitted to committee May 30, 1980.

ABSTRACT

The biological effects of tetrachloroethylene, an important industrial solvent, have been described in studies of various designs. Human experimental studies and surveys of exposed workers have noted neurological signs and symptoms of mild to moderate severity from vapor levels acceptable for the work environment. Although tetrachloroethylene is known to be lipophilic, adverse human reactions to its vapor have not been studied in relationship to the relative body fat of exposed workers. The results of a study of occupationally exposed workers are presented and analyzed in relationship to measured body fat. Proposals for further studies are suggested to investigate further the association between adverse response to tetrachloroethylene vapor exposure and subject body fat.

TABLE OF CONTENTS

LIST OF FIGURES

I INTRODUCTION

Tetrachloroethylene ($Cl_2C=CCl_2$, perchloroethylene) is a solvent widely used as a degreaser in industrial maintenance facilities and as the principal agent for commercial dry cleaning. Its use has increased during the past several years in industry because of its reported lower hepatic toxicity as compared to trichloroethylene, the solvent previously used as a degreaser. The absence of Environmental Protection Agency regulations regarding the discharge of tetrachloroethylene vapors is an added incentive for industry to use tetrachloroethylene (TCE). TCE use may also be found in the chemical industry as an intermediate substance in the manufacturing and processing of ether, drugs, rubber, soap, tar, wax, and fumigants.

Exposure can occur by inhalation of the vapors and by percutaneous absorption of the liquid with the latter causing a dermatitis but relatively little systemic intake. Of greater concern is the inhalation route as TCE is readily absorbed by the pulmonary circulation. The symptomatology and toxicity of TCE have been established by both animal and human experimental studies. Effects of acute exposure to high levels of the vapor include central nervous system depression, hepatic injury, and anesthetic death (U. S. Department of Health, Education, and Welfare, 1977). Lower level experimental exposures have resulted in malaise, vertigo, and fatigue (Kovarik, et al., 1973; Stewart, et al., 1970).

Studies of exposed workers have produced varying reports. One study, noting the neurological signs and symptoms of workers exposed to levels of 200 ppm to 2500 ppm, concluded that the symptoms were the result of inadequate or defective functioning of the liver and the suprarenal gland cortex

in response to the insult rather than to the excessive exposure to TCE *per se* (Chmielewski, *et al*., 1976).

Of greater concern is the effect upon workers who work in environments which do not exceed the established threshold limit value (TLV) of 100 ppm (670 mg/m^3) or where excursions in excess of the limits were transient, in other words, establishments which are considered to be "clean" regarding vapor control and exposure. Long term exposure to TCE in these facilities caused hemorrhagic pneumonia, pulmonary edema, liver cell necrosis, and heart muscle fat accumulation (Muenzer and Heder, 1972). Headache, fatigue, nervousness, sleepiness, vertigo, and a feeling of inebriation have been reported in surveys of workers regularly exposed to TCE vapors. One study reported 72.5% of the workers with such subjective complaints and 45% of those ill showed clinical signs of neurosis (Kovarik, *et al*, 1973). This study gains added significance since it was a survey in a Czechoslovakian industry where the TLV is about 33 ppm or one third of the United States limit. Although the study used a control group composed of workers from another branch of the industry, the accurate documentation of symptoms relating to a lack of well-being is subject to considerable bias even though the symptoms are compatible with the known effects of the solvent.

Tetrachloroethylene is known to be highly soluble in lipids. An animal study revealed marked uptake and sequestration of the solvent in the fatty tissue of rats (Savolainen, *et al*., 1977) and another study suggested that the toxicity of chlorinated hydrocarbons is related to its distribution in different types of tissue (Sato and Nakajima, 1979). Exposed workers will absorb different quantities of the solvent based on general body

size but the quantity will be directly proportional to the capacity of the metabolic and excretory systems and no significant difference in toxic effects would be expected. Solvent absorption will also be related to percent body fat where the de-toxifying mechanisms would not be directly proportional to the solvent load. Therefore, workers with the same lean body mass but with different body fat mass would be expected to respond to identical solvent exposures differently. Workers with a higher percentage of body fat may experience more symptoms or more prolonged duration of symptoms as compared to leaner co-workers due to the former having increased fatty storage of the solvent and subsequent increased internal exposure as the solvent is excreted. Conversely, high body fat may provide a protective mechanism as it competes with the central nervous system for the solvent, stores it, and excretes it at a level below the symptomatic threshold. Since it is uncertain which mechanism might take precedence, both the high percent and low percent body fat workers (or abnormal body fat collectively) should be considered to be at different risk from TCE vapor exposure. Worker surveys have not addressed body fat as a factor in tolerating exposure to TCE vapors.

It is generally recognized that workers self-select themselves among the various occupations to some degree, based on biological endowments. This is most readily observed in the occupations which require unusual strength, dexterity or intellectual ability. No less significant is the distribution resulting from biological variabilities which are less apparent but yet effectively determines occupation or job site. A worker's selection of and satisfaction at a job site is as much the result of his feeling of well-being as it is a result of his ability to master the

necessary skills and his acceptance of adequate compensation and benefits. This study attempted to determine if abnormal body fat produced sufficient feeling of lack of well-being from TCE vapor exposure to result in out-migration from that shop by susceptible workers.

This study used a one-time determination of the percent body fat of two groups of workers—one group regularly exposed to TCE vapors and another group at the same facility who had no regular occupational exposure to organic solvents. The body fat determination was based on the method of Fuchs, Theis, and Lancaster (1978) where percent body fat can be calculated from three measured parameters: body height, body weight, and the circumference of the flexed biceps (see Appendix). The percent body fat for the two groups was compared. Interpretation depended on the assumptions that: (1) workers exposed to the low level vapor concentrations allowed in industry would experience the unpleasant neurological symptoms described in the literature, (2) workers in both shops are normally distributed as to percent body fat upon entry to employment at the facility, (3) workers with abnormal body fat would be more susceptible to TCE vapors and would experience more severe or more prolonged symptoms, and (4) workers in the solvent shop will have had sufficient time to be regularly exposed to TCE vapors, to experience neurological symptoms, to make a choice regarding continuing work in that shop, and to implement a change in job location if felt necessary, i.e., that job site migration via self-selection is operative.

A difference in percent body fat between the exposed and the non-exposed groups would be suggestive that body fat is a factor in tolerating exposure to TCE vapor levels considered acceptable by industrial standards. This study serves as a preliminary indicator that body fat is a factor;

additional studies will be necessary to clarify and support any relationship that exists. Following the presentation of the results and discussion of this study, proposals are presented which could refine and expand this study to improve the quality of the results by altering the population base or the study design. A more detailed discussion of the dynamics and metabolism of TCE will follow with suggestions as to how the use of biological specimens and monitoring techniques could produce alternative study designs.

II SURVEY

A. Site and Participant Selection

The jet engine maintenance facility at Kelly Air Force Base, Texas, was selected as the study site. A relatively large group of workers was believed to be regularly exposed to TCE vapors. The shops that use TCE are not monitored for vapor concentration on a regular basis but surveys are conducted when defective machinery is suspected or altered work habits occur regarding the use of the solvent. The irregular surveys that have been conducted during normal operating conditions have shown the shops to be within the Federal standards of 100 ppm on an eight hour time-weighted average with a ceiling concentration of 200 ppm. Consultation with the Occupational Health Service at the facility revealed that no worker had been known to present to the clinic with symptoms referable to excessive TCE vapor exposure.

A preliminary walk-through of the facility was conducted to determine the sites of use of TCE, related work procedures, personnel involved, and the level of readily detectable odor of TCE during normal operating conditions. Two sites surveyed met the criteria of the study for workers regularly (daily) working with and exposed to TCE vapors. Operations involved the degreaser and decarbonizing of aircraft parts that had been previously disassembled. Parts were placed in a basket and lowered into a vapor degreaser at a controlled rate by a chain hoist. The TCE reservoir is heated to 250^{o}F and the vapors that are emitted are allowed to saturate the parts and excessive vapors are cooled and the condensed liquid TCE returns to the reservoir. Vapors that escape the cooling process rise in the

tank to be drawn off by suction rim vents which are exhausted to the outside air. The two sites selected had TCE vapors readily detectable which indicated that the concentration was at least 50 ppm. All the workers in the shops had at least several months exposure to this working environment.

The non-exposed or control group selected was workers employed in a different building where parts were prepared and arranged for reassembly. The physical exertion, job skills, and pay grades were comparable for the two groups. Only men were selected to participate since the study method for determining body fat was applicable only for men.

B. Data Collection

The data were collected by the investigator and two assistants on two consecutive workday mornings. The assistants determined the height and weight of each participant and their familiarity with the procedures required only minimal instruction. Weight was determined by a medical balance scale which was re-checked for zero indication at zero setting after each move of the equipment. In accordance with the advice of Lancaster, height was not measured by use of the scale integral with the balance scale but was determined by having the subject stand against a wall where a metric measure had been accurately placed by the investigator and read-out obtained by the position of a square block of wood which had been placed on the subject's head. Both measurements were made after the subject had removed his shoes and any protective devices such as aprons, or gloves. Weight was recorded after subtracting two kilograms for the light moderate weather clothing that the subjects were wearing.

The maximum circumference of the flexed biceps of the dominant arm was measured by the investigator with a metal metric measure after practice resulted in repeatable measurements to within 0.1 cm which was considered adequate for the study. Data was recorded to the nearest 0.1 cm for height and biceps circumference and to 0.1 kg for weight.

Data was obtained during a one time visit to each shop and participation was determined by those at work that day and who agreed to take part in the study; all workers who were previously determined to be suitable for the study and who were asked to participate agreed to take part. The exposed group included 12 workers and the non-exposed group totaled 47 workers.

III RESULTS

Figures I and II show the frequency distribution of percent body fat for the exposed and control groups respectively. The range of percent body fat found for each group was large: the exposed group had percent body fats from 5.9 to 31.0, the control group from 7.4 to 38.4. The control with the larger sample bears some resemblance to a normal distribution, with a mean of 22.6 and a standard deviation of 7.12. The distribution of the smaller exposed group shows less resemblance to a normal distribution around a mean of 23.0 with a standard deviation of 8.01.

The data of the two groups were subjected to a t-test to determine if there was any significant difference between the percent body fat distributions of the two groups. The t value of 0.169 that resulted indicated that the small differences in distribution were as likely to occur from chance as from any other mechanism altering the distribution.

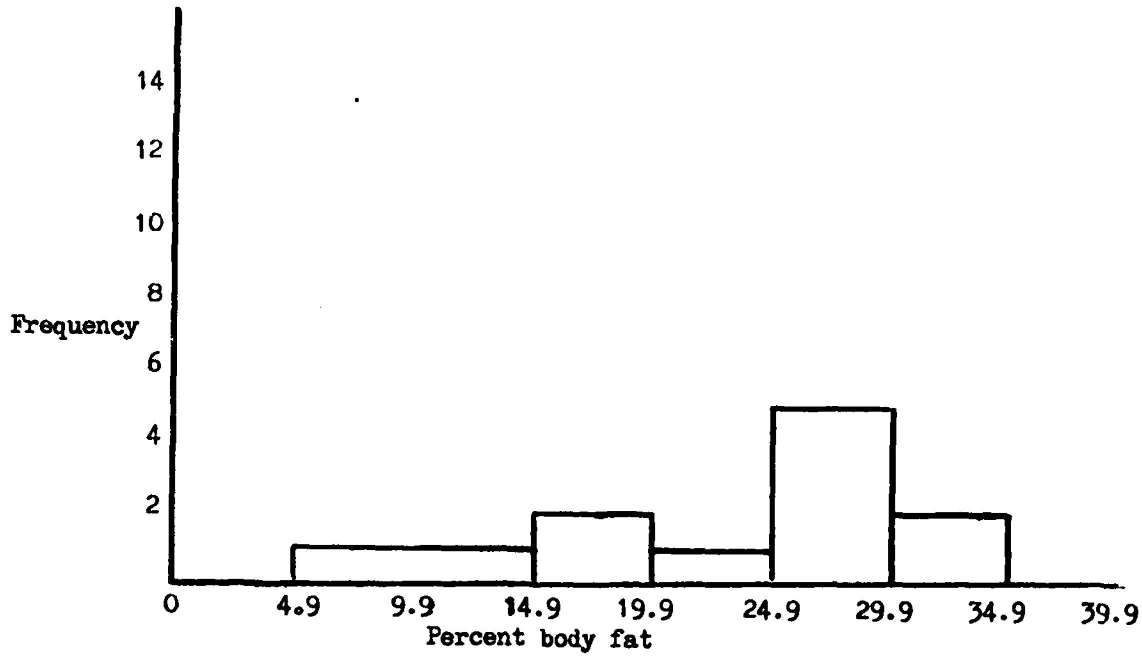

Figure I Distribution by percent body fat of workers exposed to TCE vapors

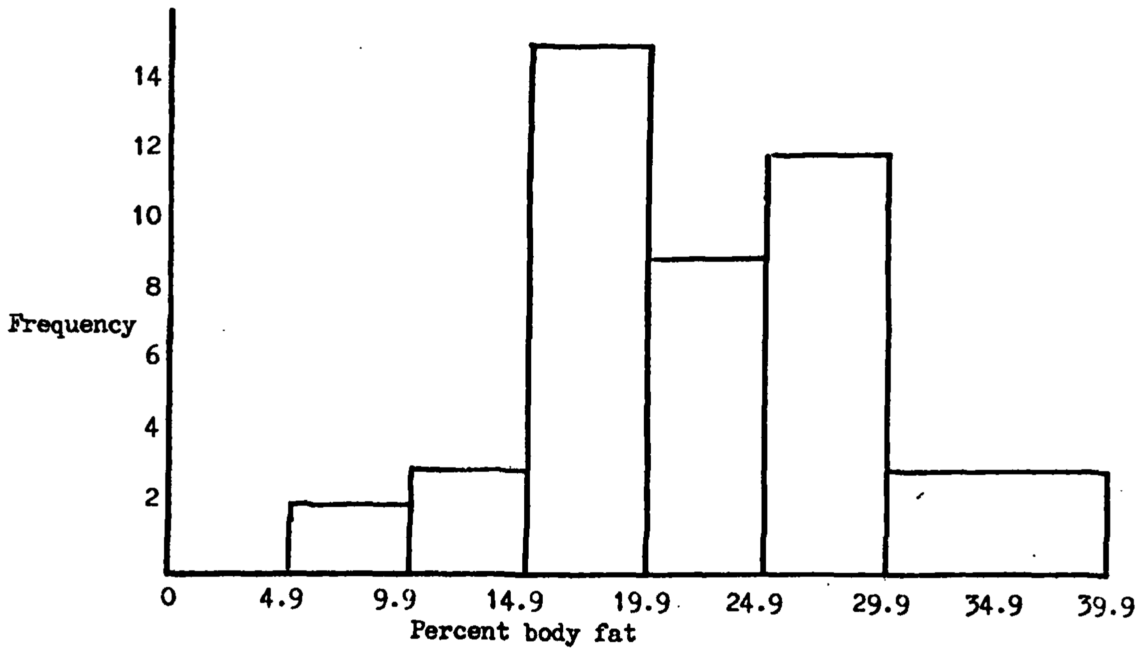

Figure II Distribution by percent body fat of workers not exposed to TCE vapors

IV DISCUSSION

The small size of the group of workers regularly exposed to TCE vapors at the facility was unexpected since a preliminary investigation indicated that 40-50 workers would be suitable for the study. Many workers had exposure to TCE but the exposure was not regular or significant, therefore it was considered necessary to eliminate from the study those workers who did not have regular daily exposure in an environment where TCE vapor was readily detectable to the investigator. This procedure resulted in a study group of only 12 workers. Such a small sample size presented a potential problem to the interpretation of the results of this study. Intuitively, a relatively small shift of percent body fat distribution between the exposed and control groups was expected. The use of the t-test, which is particularly useful in dealing with small samples, does allow the assumption that it is unlikely that any significant difference existed between the two groups in respect to percent body fat.

The assumption that affected workers with abnormal body fat after sufficient exposure to TCE vapors would self-select away from that job environment proved to elude firm or reasonable validation. Personnel and budget policies at the facility had resulted in a stable work force with very few new workers hired during the previous five years. With only a few exceptions, the workers in both groups had been on their present jobs for at least several years. Personnel records were not available to determine to what extent job mobility existed in general at the facility or for the study subjects specifically. Discussions with supervisors and personnel officials neither confirmed nor negated with reasonable certainty that the

self-selection process assumed by this study had been operative.

This study was intended to serve as a preliminary survey of a worker population to determine if such a cross-sectional survey might be effective in assessing the single dependent variable of subject percent body fat as related to exposure to TCE vapors. Despite the failure of this study to demonstrate such a relationship, the available research indicates that percent body fat as a factor in tolerating exposure to TCE vapors is a topic warranting further investigation.

As suggested above, a cross-sectional study using anthropometric data to determine percent body fat between two groups of workers may be more definitive and supportive of a hypothesis if the study sample size could be enlarged. A multiple site study might be required to acquire a population of sufficient size. The techniques of the study would not be difficult to adapt to multiple site use since the measurement procedures are easily learned and accurately performed particularly by medical technicians and therefore the techniques and data acquisition are unlikely to vary significantly among study sites. The determination of TCE vapor level in the workplace would need to be more precisely made by standardization of existing in-house procedures or by processing at a central facility. A difference in the time-weighted averages of TCE vapor levels among the sites would be helpful since a corresponding gradient of subject responses may be noted. In this respect, international studies would offer advantages since the different threshold limit values for TCE established in different countries would present a gradient of exposure levels but with each site operating at a recognized acceptable level of exposure to the worker.

The question of adequate job mobility to ensure sufficient self-selection in response to TCE vapor symptoms would present a more difficult problem in a multiple site study. In the present study, as noted, this factor could not be established with any degree of certainty. Job mobility would be the result of skill levels, training programs, company policies, and alternate job availability as determined by local economic conditions. In addition, company personnel records would be anticipated to vary widely in their usefulness to an investigator attempting to determine comparability of job mobility between the sites or to determine factors which could correct for the differences.

A shift in percent body fat distribution between an exposed and non-exposed group could also be studied using a prospective cohort design. Workers upon entry could be randomly assigned to a job with TCE vapor exposure or a job without TCE vapor exposure and their job changes and TCE vapor exposure tracked over a several year period. The two groups could then be compared. One site would be desirable if an adequate sample size became available since co-ordination with one personnel department would facilitate monitoring of job mobility and prompt assessment of related workplace factors. The anthropometric data system as used in the present study could be used since the system has adequate validity and repeatability for the purposes of the study. In addition, this technique was readily acceptable to both management and employees.

Despite explanations of the purpose and procedures of the study, many of the subjects initially perceived that the study was related to a weight study or a weight control program. It is likely that this belief would be maintained by some of the subjects in a long term prospective

study where periodic determinations of percent body fat may be required. It is conceivable that some subjects may alter their weight in response to such a belief. Therefore a second control group of randomly allocated subjects not exposed to TCE vapors should be included in the study. This group would be measured for percent body fat once at the beginning and once several years later at the termination of the study and the distribution of percent body fat would be compared with the second or serially measured control group. Lack of a significant distribution shift between the two control groups would provide reasonable assurance that mere participation in a study repeatedly measuring body parameters did not alter the dependent variable, percent body fat, since subjects measured twice during a several year interval would be unlikely to respond by altering their weight. If a shift is noted, it must be considered as a factor in evaluating any distribution shift between the serially measured study group and the serially measured control group.

However, refinements and expansion of the present study to assess health responses to low level TCE vapor by observing a shift in worker populations based on abnormal body fat may still prove insufficient to substantiate a hypothesis. Studies directly based on the dynamics of absorption and excretion, metabolism, and detoxification of TCE and employing biological specimens may prove to be more effective in assessing the role of body fat as a factor in TCE vapor tolerance. Although a complete pharmacokinetic profile of TCE as a function of dose and route of exposure is not available, sufficient knowledge regarding its physical characteristics and metabolic fate is available to aid the formulation of further studies.

Since organic solvents are generally highly volatile, research has

focused on the inhalation route of uptake, noting that the factions excreted by the lungs and the faction metabolized varied with the compound under study. The rates of absorption and subsequent excretion are largely dependent on the solubility of the vapor in the blood, which is usually expressed as the blood/air coefficient. A vapor that has a high blood/air partition coefficient is readily absorbed by the pulmonary circulation and distributed throughout the body. The excretion rate will be low since the blood will not readily release the substance and therefore the body's exposure to the solvent is prolonged. While in the body the solvent is distributed to the various body tissues and the amount taken up by each type of tissue is determined by a second partition coefficient, the tissue/blood. Generally for organic solvents, the tissue/blood partition coefficients are near or at unity with the exception of adipose tissue (Sato, et al., 1974, 1977). The adipose tissue/blood partition coefficients for organic solvents are high, usually on the order of ten to several hundred. Knowledge of these two factors, blood/air and tissue/blood partition coefficients, are useful is assessing the potential that an organic solvent has for accumulation in the body after exposure.

In vitro studies to determine oil/water partition coefficients have been used to approximate the relationships noted above. Significant correlations have been found between high oil/water partition coefficients and toxic effects as manifested by narcotic actions or ED_{50} of recognized narcotic agents (Hansch, 1971; Miller, et al., 1972). Sato and Nakajima (1979) examined the pertinent partition coefficients for twenty chlorinated hydrocarbons, including tetrachloroethylene, and concluded that the nonspecific narcotic effects of organic solvent vapors were dependent on the oil/air or

oil/water partition coefficient. In addition, they demonstrated a high correlation between the various partition coefficients and the threshold limit values for each substance, including TCE, as recommended by the American Conference of Governmental Industrial Hygienists.

Experimental human exposures to TCE vapors at various concentrations between 1,060 ppm and 106 ppm during an early study concluded that the depression of the central nervous system was the only symptom complex of concern (Rowe, et al., 1952). The study used a chamber with controlled vapor levels in which the subjects remained for varying periods, up to eight hours. Reactions to the TCE vapors were determined by observation of the subjects' behavior and motor co-ordination and by the subjective responses of the subjects. At a TCE vapor level of 106 ppm after eight hours, the subjects reported that the odor was not objectionable but some minor eye irritation was reported. Motor co-ordination, however, was determined to be unimpaired. A two hour exposure to 200 ppm resulted in eye irritation, nasal discharge, and complaints of sleepiness and dizziness. The investigators proposed 100 ppm as the maximum level for routine industrial exposure based on their results. Levels in excess of 200 ppm were not recommended because of the probability of decreased mental ability and a lessened sense of "responsibility." One hundred ppm was subsequently accepted by industry and later written into regulations by the Federal government as the TLV for TCE vapor level.

The work of Stewart, et al., (1970) expanded on that previously accomplished by Rowe. Simulated work weeks of seven hours a day for five consecutive days were spent by the subjects in a chamber with the TCE vapor level maintained at 100 ppm. The resulting signs and symptoms of the

subjects were more precisely noted and some information was obtained regarding the excretion of the solvent. Adverse effects were noted primarily during the first two hours of exposure and included mild headache (25%), mild dysphasia (25%), and sleepiness (40%). Although the subjects tended to become more tolerant of the adverse effects as the five day study progressed, the authors commented that some of the subjects appeared to be unusually susceptible to TCE under the test conditions. There was no attempt, however, to correlate the increased susceptibility with any variable. The authors noted that the solvent was exponentially excreted from the lungs with most excreted within the first 24 hours following cessation of exposure and that the metabolism of TCE was an insignificant factor in its elimination. The residual TCE after the 24 hour period was believed to be due to absorption by and slow excretion from the fatty tissue. Post-exposure alveolar concentration of TCE was noted to be increased in those with increased body mass—body fat was not a factor considered in the study as reported. In view of the information cited above regarding the partition coefficients of TCE referable to human tissue, a repetition of Stewart's study analyzed for percent body fat of the subjects would be helpful in determining the effect of percent body fat as a factor in tolerating exposure to TCE vapors.

Further studies, whether conducted in the laboratory or in the workplace, might benefit from the precision of an objective biological test to supplement the largely subjective responses which result from low level TCE vapor exposure. The National Institute for Occupational Safety and Health recommends breath analysis to evaluate exposure of workers to the solvent. Although only two percent of TCE is metabolised in the human body

(Monster, 1979), the biological half-life of trichloroacetic acid, the principal metabolite, has been measured in the urine of occupationally exposed human subjects (Ikeda, et al., 1972). Gas chromatography-mass spectrometry methods are available to accurately assess TCE and trichloroacetic acid in the urine (Braun, 1978) and such information could be useful in studies correlating the rate of decrease of residual TCE and recovery from adverse effects in subjects with normal and abnormal body fat. Accurate measurements of the solvent in expired air can be obtained by the cryogenic sampling system described by Conkle, et al. (1975). Monster and Houtkooper (1979) concluded that the best results in estimating uptake are obtained by estimations from the concentrations in blood specimens, and that including results of simultaneously measured concentrations in exhaled air or urine did not improve the estimate. The human subject chamber studies by Hake, et al.,(1976) noted that breath samples for TCE immediately post-exposure and eight and 24 hours later were accurate indicators of the amount of TCE absorbed by a subject. It is apparent from the literature that sophisticated and accurate techniques are available for measuring any of the three biological specimens and that study design and subject acceptability will dictate the methods used.

The present study assumed that adverse response to the TCE vapor exposure would produce a population less sensitive to TCE because of the ease of job mobility. Although the results on job mobility in this study are uncertain, the concept may be useful in further studies provided that the factors contributing to job changes are appropriately considered. A job change is the result of job dissatisfaction, broadly interpreted. Relevant factors include unpleasant work tasks or working conditions, unsatis-

fying relationships with supervisors or fellow workers, dissatisfaction with the opportunities for advancement in job status or benefits and, of course, the expectation that a change will result in improvement in one, several or all of these factors. Tetrachloroethylene vapor exposure could be one element contributing to an unpleasant work environment. The present study used study and control populations which performed comparable physical tasks which were at a semi-skilled level. The samples selected produced groups which performed similar tasks, in similar environments and working conditions (with the exception of the TCE exposure), for the same pay, benefits, and opportunities for advancement. The ability to match the groups was facilitated by using a single facility for the study and would lend support to a single site study being the most desirable for this type of study. Job changes due to dissatisfaction with the work tasks, environment, and opportunities for advancement, is probably less significant than intuitively conceived by a professional or an investigator since semi-skilled workers often are more job stable than the more skilled or professional workers. The remaining potential variables, unsatisfying relationships with supervisors or fellow workers may be more difficult factors to match. The determination of the relation of job changes to these factors could be made by observation, interviews or questionaires designed to evaluate each workplace or each worker out-migrating from a TCE environment. However, this approach would be time-consuming and vulnerable to mis-classification because of the subjective nature of the evaluation. In addition, the intervention necessary to make the assessment might alter the relationship under examination by making the supervisor or the worker more aware of

the significance of the event, possibly causing a reversal of the employee's decision and/or the supervisor's future relationships with employees in that shop. This would introduce a new and probably unmanageable variable into the assessment of job mobility.

Although human behavior and relationships are the product of a multitude of factors, many difficult to quantify, each individual is usually consistent in his response to certain situations or environments. For example, the best predictor of future success or failure in an academic program is the past history of success or failure. Likewise, the best predictor of success on a job or with significant relationships is a past history of such success. This consistency of human behavior can be applied to a study where job mobility resulting from dissatisfying relationships with supervisors or fellow workers needs to be recognized and compensated for in the analysis of the data. A worker known to have made frequent job changes in the past would not be accepted into the study group since a job change by this worker would likely be due to reasons other than adverse effects from TCE vapor exposure. For the purposes of the study it is unnecessary to determine specifically why this worker did change jobs. The necessary job history information would be available through the personnel record already used to track the worker at the facility. Although some valid adverse responders to TCE vapors may be eliminated from the study by this method, the study would be improved in quality since greater confidence could be placed in the mechanism of job change as a reaction to TCE exposure.

It can be seen that a number of different approaches of study design could prove effective in elucidating a relationship between body

fat and tolerance to TCE vapors. Experimental studies with human subjects exposed to controlled vapor concentrations in chambers could be done to measure the subjects' objective and subjective reactions. However, a knowledge of the vapor concentration to which the subject was exposed would not be sufficient to determine the internal concentration of the solvent that would act upon the central nervous system. Variations will be produced by differences in the minute respiratory volume (Hake, et al., 1976) resulting from different levels of activity and, more important for the purpose of this paper, by the percent body fat. As noted, several laboratory tests of biological specimens are available to assess accurately the actual internal levels of the solvent. Although terminal expiratory phase breath, urine, and blood all reflect the level of internal solvent, the blood specimen would appear to be preferable since it would sample the substance in the most direct contact with the target of concern, the central nervous system. In addition, data on blood specimens may prove of value to future researchers who may approach the problem by studying the blood/fatty tissue or blood/nervous system interfaces. However, repeated blood specimens may be less acceptable to subjects particularly outside of the short-term laboratory study setting. With data available regarding TCE vapor concentration exposure, solvent absorbed, and central nervous system symptoms and signs for each subject, the percent body fat could then be measured for each subject using the biceps[2] method or other technique (see Appendix). The data would be analyzed to determine if a relationship existed between severity or duration of adverse effects and percent body fat for subjects with comparable blood concentrations of TCE.

A workplace study, although more difficult to control, can also be

of value. The subjects are studied in the environment of concern while performing the tasks normally associated with the job. The latter is important since Hake, et al. (1976) demonstrated that the amount of TCE absorbed was directly related to respiratory minute volume which in turn was related to activity. Provided that a suitable stable worker population is available, a workplace study can be developed into a long-term project, possibly as part of an existing Occupational Health program. This attribute is of particular value where the effects may be subtle and not readily attributed to the workplace by the worker.

The results of the present study and the information presented in this discussion indicate that a more comprehensive workplace study is an appropriate method to investigate the relationship between TCE vapor exposure and percent body fat. The study preferably would use a single industrial facility where a significant number of employees have regular exposure to TCE vapor in a work environment where the TLV is not being exceeded. A review of the periodic surveys for TCE vapor levels by the Occupational Hygiene Department would be necessary to confirm compliance with the standard. The skill level, physical tasks, and pay level for the jobs where the TCE use meets the requirements of the study will be determined and matched with two other shops where exposure to organic solvents does not occur. Coordination with the personnel department would be established to review the records and job histories of those entering employment at the facility in the shops previously established as participating in the study. Workers who had changed jobs in excess of three times during the preceding five year period would not be accepted for the study. The remaining workers should be randomly allocated to the three shops to comprise the exposure

group and the two non-exposure groups. The subjects' personnel records will be identified as to their participation in the study and arrangements made to inform the investigator when a subject changes job location. When a change does occur, sufficient information must be available in the records to determine if a skill level or pay level changes were factors in the change since either would eliminate the subject from the study.

Percent body fat would be determined for subjects in all three groups upon entry into the study. The preferred method would be the biceps[2] method of Fuchs and Lancaster since it is well suited to field studies and has adequate validity. The required measurements would be obtained semi-annually, when possible at the time of any required periodic physical examination, for the study group and the first control group. The second control group will have a repeat measurement at the termination of the study, tentatively projected at three years. The duration of the study, however, would be dependent on the flow of workers into the facility generating a sufficient sample size over time. As the study is extended, the investigator must assure that the work procedures, TCE use, or other parameters in the shops under study are not being altered.

The subjects in the study group would be tested at regular intervals for absorbed TCE levels. End tidal breath samples would be collected in the workplace one to two hours before the end of the last shift of the work week to allow each subject to reach his maximum saturation with the solvent. Concentrations of solvent will vary for the subjects based on their percent body fat and because it is unlikely that each worker would be exposed to identical vapor levels during the course of the workday.

Analysis of the data would focus primarily on determining if a

shift in distribution of body fat for the study group had occurred in comparison to the control group, the normally distributed body fat sample. The direction and magnitude of the shift, if statistically significant, would substantiate the hypothesis that abnormal body fat is a factor in tolerating exposure to TCE vapors. The TCE breath sample data would be analyzed to determine if an association exists between concentration and percent body fat. Such an association, in conjunction with an association with an out-migration from the TCE shop would significantly substantiate the hypothesis since a gradient of response would become apparent.

V CONCLUSION

Industrial hygiene and occupational health disciplines have tended to be primarily concerned with the physical and chemical techniques for the assessment of a workplace as being acceptable or unacceptable. The body of literature describing the pathology that results when workers are exposed to unsafe conditions is extensive and important. However, preoccupation with TLVs or other environmental measurements and classical occupational diseases may obscure the recognition of more subtle adverse occupational effects (Hatch, 1974). Individual workers bring to their respective jobs a wide variety of strengths and weaknesses, from muscular power to a different capacity to produce an important liver enzyme. Depending on the stresses of his specific workplace, such biological differences may produce varying degrees of susceptibility to or protection from the adverse effects from exposure to the stress. When the biological differences are within the normal distribution for the worker population, the adverse effects are likely to be attributed to inadvertent or undetected excessive exposure.

The results of a study which attempted to detect subtle but important adverse effects to a common industrial solvent in relation to a normally distributed biological variable, body fat, was presented. Suggestions are offered for further more definitive investigations. Although job mobility, as a self-selection process, is assumed to operate in general, particular factors regarding the worker and the social or economic situations may impair the efficiency of this process. The result may be a prevalence of ill health, subtle in nature but still a considerable burden to the employer-employee community.

APPENDIX

The method used to determine percent body fat is based on the procedure developed and reported by Fuchs, Theis, and Lancaster (1978). The system used three measurements: height, weight, and the maximum flexed-biceps circumference of the dominant arm. Percent body fat was then calculated from the equation:

Percent Body Fat =

$$\frac{\text{Wt(kg)} - 0.5143 \times \text{Ht(cm)} - 0.01783 \times \text{Biceps circum.(cm)}^2 + 49.67}{\text{Wt(kg)}} \times 100$$

The technique evolved from data collected on 198 men who were also measured by the tritium dilution method. The equation was validated on an additional 65 men, comparing measurements obtained by tritium dilution ($r = 0.91$), K^{40} wholebody counter technique ($r = 0.90$), and the water displacement method ($r = 0.86$). The method devised by Fuchs, et al. is often called the biceps^2 technique and is well suited to field studies, requires minimal training, and uses readily obtainable equipment.

BIBLIOGRAPHY

Braun, H. 1978. Gas chromatographic-mass spectrometric method for the determination of perchloroethylene and its major metabolites in urine. Journal of Chromatography 150, 212-215.

Chmielewski, J., Tomaszewski, R., Glombiowski, P., Kowalewski, W., Kwiatkowski, S. R., Szczekocki, W., and Winnicka, A. 1976. Clinical observations of the occupational exposure to tetrachloroethylene. Bulletin of the Institute of Maritime and Tropical Medicine 27, 197-205.

Conkle, J. P., Camp, B. J., and Welch, B. E. 1975. Trace composition of human respiratory gas. Archives of Environmental Health 30, 290-295.

Fuchs, R. J., Theis, C. F., and Lancaster, M. C. 1978. A nomogram to predict lean body mass in men. American Journal of Clinical Nutrition 31, 673-678.

Hake, C. L., Stewart, R. D., Wu, A., and Graff, S. A. 1976. Experimental human exposures to perchloroethylene, part I, absorption and excretion. Toxicology and Applied Pharmacology 37, 175.

Hansch, C. 1971. Quantitative structure-activity relationship in drug design. In Drug Design, Ariens, E. J., (Ed.), Vol. 1, 272-273.

Hatch, T. F. 1974. Priorities in preventive medicine. Archives of Environmental Health 29, 52-55.

Ikeda, M., Ohtsuji, H., Imamura, T., and Kokoike, H. 1972. Biological half-life of trichloroethylene and tetrachloroethylene in human subjects. British Journal of Industrial Medicine 29, 328.

Kovarik, J., Medek, V., and Borovska, D. 1973. Perchloroethylene from the neurological standpoint. Annals of the Academy of Medicine (Lodz) 14, 49-54.

Miller, K. W., Paton, W. D. M., Smith, E. B., and Smith, R. A. 1972. Physicochemical approaches to the mode of action of general anesthetics. Anesthesiology 36, 339-351.

Monster, A. C. 1979. Difference in uptake, elimination, and metabolism in exposure to trichloroethylene, 1,1,1-trichloroethane and tetrachloroethylene. International Archives of Occupational and Environmental Health, 42, 311-318.

Monster, A. C., and Houtkooper, J. M. 1979. Estimation of individual uptake of trichloroethylene, 1,1,1-trichloroethane, and tetrachloroethylene from biological parameters. International Archives of Occupational and Environmental Health 42, 319-324.

Muenzer, M., and Heder, K. 1972. Results of an occupational, medical and technical survey of chemical dry cleaning establishments. Zentralblat fuer Arbeitmedizin und Arbeitsschutz 22, 133-138.

Rowe, V. K., McCollister, D. D., Spencer, H. C., Adams, E. M., and Irish, D. D. 1952. Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects. Archives of Industrial Hygiene and Occupational Medicine 5, 566-579.

Sato, A., and Nakajima, T. 1979. A structure-activity relationship of some chlorinated hydrocarbons. Archives of Environmental Health 34, 69-75.

Sato, A., Nakajima, T., Fujiwara, Y., and Hirosawa, K. 1974. Pharmacokinetics of benzene and toluene. International Archives of Arbeitsmedizin 33, 169-182.

Sato, A., Nakajima, T., Fujiwara, Y., and Murayama, N. 1977. A pharmacokinetic model to study the excretion of trichloroethylene and its metabolites after inhalation exposure. British Journal of Industrial Medicine 34, 56-63.

Savolainen, H., Pfäffli, P., Tengen, M., and Vainio, H. 1977. Biochemical and behavioral effects of inhalation exposure to tetrachloroethylene and dichloromethane. Journal of Neuropathology and Experimental Neurology 36, 941-949.

Stewart, R. D., Baretta, E. D., Dodd, H. C., and Torkelson, T. R. 1970. Experimental human exposure to tetrachloroethylene. Archives of Environmental Health 20, 224-229.

United States Department of Health, Education, and Welfare. 1977. Occupational Diseases, Revised Edition, 213-215.